Citation:

Mosdøl A, Witte DR, Frost G, Marmot MG, Brunner EJ. Dietary glycemic index and glycemic load are associated with high-density-lipoprotein cholesterol at baseline but not with increased risk of diabetes in the Whitehall II study. *Am J Clin Nutr.* 2007;86(4):988-94.

PubMed ID: 17921375

Study Design:

Prospective cohort

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

The purpose of the study was to investigate whether dietary glycemic index (GI) and glycemic load (GL) are associated with clinical risk factors at baseline and with incident type 2 diabetes mellitus using healthy participants from the Whitehall II study.

Inclusion Criteria:

- Participants in the Whitehall II study in beginning in 1985 who, during phase three of the study, completed the detailed dietary questionnaire or attended the research clinic as required
- White participants
- Informed consent was taken at baseline and renewed at each point of contact throughout the study

Exclusion Criteria:

- Participants in the Whitehall II study who at phase three did not either complete the food frequency questionnaire or attend the research clinic
- Ethnic minority participants excluded because FFQ was designed for Western diets.
- History or diagnosis of diabetes at the phase three screening

Description of Study Protocol:

Recruitment

- Participants were recruited from 20 civil service departments in London, England.

Design

- One cohort of non-diabetic, eligible participants from the Whitehall II study were examined at phase three (considered baseline for current study)
    - GI and GL were assessed at baseline from food frequency questionnaires (FFQ), divided into tertiles, and compared to participants' baseline characteristics.
    - GI and GL were compared to blood measurements of HDL, triacylglycerols, fasting glucose, fasting insulin and 2-hour glucose.
    - Linear regression models with clinical measures as outcome variables according to levels of GI and CL were calculated.
- Participants were followed up every 2.5 years with a FFQ and received clinical examinations in 1991-1994 (phase three/baseline for current study), 1997-1999 (phase five), and 2003-2004 (phase 7).
- Participants were followed for the duration of the Whitehall II study, or until the outcome of incident diabetes.
    - Hazard ratios of incident diabetes were examined across sex-specific tertiles of GI and GL.

Statistical Analysis

- All nutrient intake was adjusted for energy by the residuals method. Participants were ranked and divided into sex-specific tertiles of dietary GI and GL.
- Mean values of clinical measures were age adjusted with age groups as a covariate and the logarithmic terms that resulted of the clinical measures were exponentiated.
- Univariate analysis of variance was used to analyze linear trends of continuous variables and chi-square linear-by-linear associations for trends in proportions.
- This was repeated for interaction terms, and if significant, with values for trend were presented with each sex separately. Otherwise, trends were analyzed by the whole sample with sex as a covariate.
- Linear regression was used to analyze associations between dietary GI and GL and the clinical measures were adjusted for sex, age, and energy misreporting.
- Cox proportional hazards regression models were used.

Data Collection Summary:

Timing of Measurements

- A 127 item Food Frequency Questionnaire (FFQ) was administered at baseline
    - GI and GL were calculated
        - GI: Used the 2002 international table of GI values of foods; average dietary GI was calculated by adding the product of the carbohydrate content multiplied by the portion size, frequency of use, and GI value of the food and dividing the sum by the total carbohydrate intake
        - GL: Calculated by the total carbohydrate intake multiplied by the dietary GI divided by 100
- Fasting blood sample was taken at baseline along with a 2-hour follow-up blood sample

Dependent Variables

- Subjects were monitored for incident diabetes
    - Self-report of doctor's diagnosis and diabetic medication at phase one and subsequent study phases and by a 2-hour oral glucose tolerance test at phases 3, 5 and 7

Description of Actual Data Sample:

Initial N: Initial N=7321 (5175 males, 2146 females)

Attrition (final N): Final N=5598 (3969 males, 1629 females)

Age:Range from 39-63 years of age

Ethnicity: White

Other relevant demographics:

- Participants with high dietary GI were more likely to be smokers and less likely to be physically active and more likely to have an administrative (higher) job grade.
- Participants with high GL was likely to have fewer smokers and also likely to have a less administrative (lower) job grade.

Anthropometrics (e.g., were groups same or different on important measures)

Location:Participants recruited from within civil service jobs in London, England

Summary of Results:

Key findings:

- Dietary GI was not associated with the risk of incident diabetes.
- Hazard ratios across tertiles of GL showed an inverse association with diabetes risk after adjusted for sex, age group, and ratio of reported energy intake to estimated energy expenditure (P for trend =0.011).

Baseline characteristics by tertiles of energy-adjusted average GI and GL

- EI:EE did not vary across tertiles of GI and GL
- Dietary GI was weakly associated with:
    - total carbohydrate
    - fat
- Dietary GI was strongly associated with:
    - smokers
    - less physically active
    - less likely to have an administrative grade
- Dietary GL was strongly associated with:
    - total carbohydrate
    - fiber
    - inversely with fat
- High GL was associated with:
    - lower proportion of smokers
    - lower proportion of administrative grade
- Both dietary GI and GL
    - WHR had slight inverse trend

Age-adjusted means on blood tests (HDL, triacylglycerols, glucose, insulin, and 2-hour

postload glucose in low-, medium- and high- dietary GI and GL

- Significant inverse trends for HDL with higher values of dietary GI and GL
- Significant increasing trend in triacylglycerols with higher GI; no association across lower tertiles
- Lower fasting glucose concentrations and higher 2-hour postload glucose were seen with increasing dietary GI and GL, apart from dietary GI and fasting glucose among women
- Fasting insulin was inversely related to dietary GL only

Linear regression models

- Significant inverse association between GI and GL with HDL (after adjustment for employment grade, physical activity, smoking status, and alcohol intake) but noted to be attenuated after fiber and carbohydrate adjustments
- In triacylglycerols, direct associations with dietary GI were significant with model 3 (adjustments for fiber and carbohydrate intakes). Further adjustment with BMI and WHR strengthened the associations between the dietary GI and GL with HDL and triacylglycerols
- Some associations between GI or GL and measured glycemia were robust to statistical adjustments
- The relation between dietary GI and 2-hour postload glucose was significant in all models tested

Incident diabetes and hazard ratios

- After 65,774 person-years of follow-up, 329 incident cases of diabetes were identified among participants with dietary assessments
- Dietary GI was not associated with the risk of incident diabetes.
- Hazard ratios across tertiles of GL demonstrated an inverse association with diabetes risk in the base model
- A weak protective effect of high GL was not significant after adjustments

Author Conclusion:

The current study could not confirm that high dietary GI or GL diets are associated with an increased risk of type 2 diabetes mellitus despite the anticipated link with a higher risk lipoprotein profile. Whether the mulitfactorial concept of GI is useful in studies pertaining to carbohydrate metabolism and disease risk remains uncertain.

Reviewer Comments:

- *All ethnicities were excluded based on the use of a food frequency questionnaire designed for a Western diet. Assumes that all ethnicites enrolled in the study in this international city follow non-western diet. Other ethnicities should be studied.*
- *Did not identify attrition from the study, or participants who dropped out or discontinued over the 13 years of monitoring for incident diabetes. Subtracted final assessment of diabetes from N of initial enrollment to calculate 76% attrition rate.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	No
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	N/A
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	No
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A

3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	No
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	No
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	No
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes

6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	N/A
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes

8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes